COMPOUNDING, CONTEMPORARY

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INTRODUCTION

Pharmacists are unique professionals—they are well trained in the natural, physical, and medical sciences and sensitized to the potential tragedy that may result from a single mistake that can occur in the daily practice of their profession. The demonstrated expertise, demeanor, and manner in which pharmacists have practiced over the years has resulted in a continued rating of pharmacists as the most respected and trusted individuals in our society. Pharmacists have the reputation of being available (in the local community) by interacting with patients, providing needed medications, and working with patients to regain or maintain a certain standard or quality of health, as well as just being there in time of need.

Pharmacy is a complex mixture of different practices and practice sites. No longer is pharmacy simply community pharmacy or hospital pharmacy. Pharmacy is diverse and offers many opportunities for those willing to look around, find their niche, and practice pharmacy to meet the needs of their own community of patients. Pharmaceutical compounding is an area that is rapidly growing and providing needed products and services to patients and healthcare practitioners. Most compounding pharmacists appear to be very interested and excited about their practices. In fact, many pharmacists intimately involved in pharmaceutical care have now realized the importance of providing individualized patient care through the preparation of patient specific products. Compounding is a professional prerogative that pharmacists have performed since the beginning of the profession. Even today, definitions of pharmacy include the "preparation of drugs" (1, 2).

> Pharmacy is the art or practice of preparing and preserving drugs, and of compounding and dispensing medicines according to the prescriptions of physicians (3).

Compounding has always been a basic part of pharmacy practice; the drugs, dosage forms, and equipment/techniques used are the variables. Pharmacists possess knowledge and skills that are unique and not duplicated by any other profession. Pharmacy activities that individualize patient therapy include compounding and clinical functions; either activity in the absence of the other results in placing pharmacy in a disadvantaged position. It is important to utilize a pharmacist's expertise to adjust dosage quantities, frequencies and even dosage forms for enhanced compliance. All pharmacists should understand the options presented by compounding.

Pharmaceutical compounding is increasing dramatically due to the impact of home health care, nonavailable drug products (especially pediatric formulations), orphan drugs, veterinary compounding, and biotechnology-derived drug products. Newly evolving dosage forms and therapeutic approaches suggest that compounding of pharmaceuticals and related products specifically for individual patients will become even more common in pharmacy practice.

A pharmacy compounder may be defined as a pharmacist who actively promotes and provides prescription-compounding services for the express purpose of attracting this type of prescription to his or her practice. One of the responsibilities of a compounder requires that the pharmacist become actively engaged in the clinical assessment of a patient in order to assist the prescriber in determining the customized patient-specific formula to be extemporaneously compounded. In addition, this responsibility requires the pharmacist to interact with prescribers and the patient when the customized formulation and dosage form are determined. Previous studies have identified the use of clinical skills and physician/patient interaction as intrinsic factors that enhance a pharmacist's job satisfaction (4–7). Therefore, a compounder who utilizes clinical skills and interacts with prescribers and patients is usually predisposed to a higher job satisfaction than would be a noncompounder whose responsibilities may not require such activities (8).

Pharmaceutical compounding requires the use of one's training in mathematics, science, and technology more than many other practices of pharmacy. It has been stated:

> The sciences are what support pharmacy's expertise in drug distribution and drug use. Recent history leads one to question whether we in the profession, and some in pharmaceutical education, recognize

> and appreciate the contribution that the pharmaceutical sciences have made and continue to make to the pharmacy profession and health care. The pharmaceutical sciences are what make us unique. They provide us the special value that we bring to the bedside. No other health professional is capable of bringing to the pharmacotherapeutic decision-making table such concepts as pH, particle size, partition coefficient, protein binding, structure–activity relationships, economics, and epidemiology. The pharmaceutical sciences, combined with pharmacy's infrastructure including pharmaceutical education, are what make the pharmacist an indispensable participant on the health care team (9).

Furthermore, what area of pharmacy practice has the opportunity of using the scientific education and training as much as pharmacists involved in individualizing patient care through extemporaneous compounding? The pharmaceutical sciences, especially chemistry and pharmaceutics, serve as the foundation for pharmacists' ability to formulate specific dosage forms to meet patients' needs.

DEFINITION OF COMPOUNDING

The National Association of Boards of Pharmacy has defined compounding as the following:

> Compounding means the preparation, mixing, assembling, packaging, or labeling of a drug or device (i) as the result of a practitioner's prescription drug order or—initiative based on the pharmacist/patient/prescriber relationship in the course of professional practice, or (ii) for the purpose of, as an incident to research, teaching, or chemical analysis and not for sale or dispensing. Compounding also includes the preparation of drugs and devices in anticipation of prescription drug orders based on routine, regularly observed patterns (10).

Compounding may hold different meanings to different pharmacists. It may mean the preparation of oral liquids, topicals, and suppositories. It may include the conversion of one dose or dosage form into another, the preparation of select dosage forms from bulk chemicals, the preparation of intravenous (IV) admixtures, parenteral nutrition solutions, pediatric dosage forms from adult dosage forms, the preparation of radioactive isotopes, or the preparation of cassettes, syringes, and other devices with drugs for administration in the home setting.

TYPES OF COMPOUNDING

Ambulatory Care Compounding

If one is able to walk, the person is considered mobile or ambulatory, i.e., the individual is not bedridden. Consequently, most pharmacists are involved in ambulatory care and most ambulatory patients are outpatients. The term actually can also be applied to home care patients and even institutionalized patients that are mobile. Ambulatory patients are generally responsible for obtaining their own medication, storing it, preparing it (if necessary), and taking it (11). It seems almost incongruous that in healthcare today, as we become more aware that patients are "individuals," respond as "individuals," and must be treated as "individuals," some healthcare providers appear to be grouping patients into "categories" for treatment and "categories" for reimbursement from third parties. Furthermore, they determine "categories" for levels of care in managed care organizations and use "categorized" fixed-dose products provided by pharmaceutical manufacturers that are available because the marketing demand is sufficiently high to justify their manufacture and production. Since when does the availability, or lack of availability, of a specific commercially available product dictate the therapy of a patient?

Pharmacists have an opportunity to extend their activities in patient care as the emphasis continues to shift from inpatient care to ambulatory care. Ambulatory care can generally encourage a team approach to health improvement, prevention, health maintenance, risk assessment, early detection, management, curative therapy, and rehabilitation (12). Ambulatory care offers a variety of opportunities for individualizing patient care through pharmaceutical compounding. In fact, it is the area where most compounding pharmacists practice.

The pharmacist's role in ambulatory care patients can include the following: 1) dispensing; 2) compounding; 3) counseling; 4) minimizing medication errors; 5) compliance enhancement; 6) therapeutic drug monitoring; and 7) minimizing expenditures (11–13). Most reimbursement for ambulatory patients comes from the dispensing or compounding process. Little financial consideration is given to counseling, minimizing medication errors, compliance enhancement, therapeutic monitoring and minimizing expenditures; however, these

activities are important and should be done. Due to the unique nature of compounded medications, counseling is an absolute must for these patients. From the previous discussion of the activities of an ambulatory care pharmacist, it should be evident that extemporaneous compounding can be vitally important in ambulatory patient care.

Institutional Pharmacy Compounding

The ever-present responsibility of the health care industry is to provide the best available care for the patient, using the best means to do so, and to provide that care in a conducive environment. This requires cooperation on the part of the institutional administration, the medical staff, and the employees (nurses and pharmacists in particular as regards to medication usage). It also must involve the patient. One of the effective means by which institutions, and therefore institutional pharmacies, can meet these challenges is to consider expanding extemporaneous compounding services within the institutional pharmacy. Pharmaceutical care and pharmaceutical compounding can provide cost savings to the institution while providing needed options to the physician through problem-solving approaches, and stimulating the institutional pharmacist through new challenges that allow the expression of both their skills and their art.

Institutional pharmacists have always been actively involved in compounding, or producing medications for the patient. Daily IV therapy is provided through compounding of medications. Antibiotic piggybacks, total parenteral nutrition (TPN) solutions, IV additives, and many others are daily calculated, compounded, dispensed, and generally administered by the nursing staff. The preparation of pediatric dosage forms also has been an area of extensive activity in some institutions.

Members of the institutional staff are constantly reading journal articles and are generally aware of innovative thought and practice by their peers. When physicians become aware of the skill, availability, and awareness of pharmaceutical compounding and that they can literally have almost any medication they need, in the form and strength needed for a specific situation, they generally request it more often. As the institutional pharmacy staff demonstrates their expertise and problem-solving skills, the medical staff consistently calls upon them (14).

In the consideration of meeting patient-specific needs, the institutional pharmacist must look at various modalities as potential solutions. When traditional institutional processes and procedures are not meeting patients' needs, extemporaneous compounding should be a consideration. Improving outcomes and getting patients well and out of the institution as quickly as possible should be the end goal. Individualized dosage forms, dosage strengths, and alternative routes of administration can often help attain these goals. Improving outcomes will assist the medical staff by allowing them to spend their time dealing with new problems as the hospital pharmacy meets the challenge of past problems. Nursing and pharmacy will have an enhanced opportunity to interest and use the skills they have developed, and provide opportunities for pharmacy to have more patient involvement and job satisfaction.

Veterinary Compounding

The first symposium on veterinary compounding, which occurred in September 1993, was a significant forum for discussion by experts and was a pivotal point in the history of veterinary compounding (15). The meeting was important since it assembled an impressive group of experts on veterinary compounding, who then set about explaining and defining the roles of the veterinarian and the pharmacist.

The Food and Drug Administration's (FDA's) interest in compounding by veterinarians dates back to the beginning of the 1990s. The avowed purpose of the symposium was to provide a forum for a comprehensive, public debate in response to the American Veterinary Medical Association (AVMA) position on compounding prior to the issuance of the FDA Compliance Policy Guide on veterinary compounding. Numerous speakers presented views on compounding by veterinarians and compounding for veterinarians by pharmacists. Topics such as conflicts of interest, lack of compounding training by veterinarians, the "new drug" issue, and bioequivalency standards were discussed in detail.

There are many reasons why veterinary compounding is necessary. For example, with multiple species ranging from very small to extremely large, it would be impossible to practice effective medicine without compounded products! Do we simply refuse to treat exotic species or very small animals? Do we abandon oncology in veterinary medicine?

Also, a more specific area of need is the lack of an ideal anesthetic drug, which has led veterinarians to devise anesthetic combinations that induce good-quality anesthesia with minimal risk to the patient. Compounding is essential for safe and effective veterinary anesthetic practice. Veterinarians need to administer anesthetic drugs to a wide variety of patients with a wide variety of temperaments, in settings that are less than ideal.

Veterinarians are called upon to anesthetize elephants, gorillas, tigers, ostriches, sharks, horses, cows, and poisonous snakes, among others. Other reasons why veterinary compounding is necessary includes: 1) the necessity for multiple injections in the absence of a compounded product; 2) rapid changes in management and disease problems in veterinary medicine; 3) problems associated with the treatment of large numbers of animals with several drugs within a short period of time; 4) cost-prohibitive factors associated with the very large volume of some large-volume parenterals required for animals; and 5) the need for previously prepared antidotes for use in cases of animal poisoning.

Unique aspects of veterinary compounding, as compared to compounding for human patients, include the potential impact on human health of compounded veterinary products in food animals, and variability in animal response and size.

The 1993 symposium expressed the following ideas: 1) veterinarians have a definite need for drug compounding; 2) drug compounding was reported to be necessary in all areas of veterinary medicine; 3) the necessity of compounding poisoning antidotes (e.g., sodium nitrite, sodium thiosulfate, methylene blue, and calcium EDTA).

Veterinary compounding will continue to exist in the future for the same reason as it does now—to fill therapeutic needs in veterinary medicine, as well as in medicine for human patients. Difficulties and costs associated with the veterinary drug-approval process will make compounding necessary to fill therapeutic needs not being met by the introduction of therapeutic agents. An increasing interdependence between the veterinarian and the pharmacist is developing, which will result in higher standards of veterinary care (15).

Nuclear Pharmacy Compounding

Nuclear pharmacy is a specialty practice of pharmacy defined as a patient-oriented service that embodies the scientific knowledge and professional judgment required to improve and promote health through assurance of the safe and efficacious use of radioactive drugs for diagnosis and therapy (16). Radioactive drugs, commonly referred to as radiopharmaceuticals, are a special class of drugs regulated by the FDA. They are unique in that they contain an unstable nuclide (radioactive nuclide) as a part of the compound designed to localize in an organ or tissue. Since radiopharmaceuticals are radioactive, the Nuclear Regulatory Commission, or a similar state agency, is involved in regulatory matters relevant to radiopharmaceuticals.

Most radioactive nuclides employed in radiopharmaceuticals have a short half-life. This is beneficial to the patient, as the total number of radioactive atoms given to the patient to produce an image will be small when the half-life of the radioactive nuclide is short, as compared to longer half-life radioactive nuclides. Fewer total atoms reduce the radiation dose to the patient and thus, the risk from a nuclear medicine procedure. However, the short half-life of the radioactive nuclide results in a short shelf-life for the radiopharmaceutical. As a result, most radiopharmaceuticals are compounded on a daily basis. The most common radioactive nuclide used in the preparation of radiopharmaceuticals is technetium-99m (Tc-99m). Tc-99m has a half-life of 6 h and emits only gamma radiation with an energy almost ideal for detection.

A nuclear pharmacist is expert at preparing (compounding) radiopharmaceuticals with Tc-99m sodium pertechnetate and reagent kits. The kits are multidose vials that contain the compound to be "labeled" with the radioactive nuclide Tc-99m in order to create the radiopharmaceutical. The contents within the vial are sterile and pyrogen free, as is the Tc-99m sodium pertechnetate. Most radiopharmaceuticals are administered intravenously so a nuclear pharmacist is expert at maintaining aseptic conditions during compounding.

The most common setting for the provision of radiopharmaceuticals by nuclear pharmacists is a commercially centralized nuclear pharmacy. Radiopharmaceuticals are prepared early in the morning (2:00–3:00 A.M.) and unit doses are delivered by automobile to hospitals near the nuclear pharmacy.

Today, there are several hundred commercial centralized nuclear pharmacies that provide a large percentage of radiopharmaceuticals used in nuclear medicine procedures. What started as limited service in large medical centers and universities by a few pharmacists with education beyond the Bachelor of Pharmacy degree has grown to extensive services provided by several hundred first professional degree pharmacists. This is truly a remarkable change in a time period of 20–25 years, and has resulted from dedicated entrepreneurs who work to make a difference in patient care through quality products and pharmaceutical care.

HISTORY OF COMPOUNDING

The heritage of pharmacy, spanning some 5000 years, has centered around the provision of pharmaceutical products for patients. Pharmacists are the only health professional who possess the knowledge and skill required to compound and prepare medications to meet the unique

needs of patients. The responsibility to extemporaneously compound safe, effective prescription products for patients who require special care is fundamental to the profession.

The 19th century did not see an end to the art of compounding, but the art did give way, however grudgingly, to new technology. According to estimates, a "broad knowledge of compounding" was still essential for 80% of the prescriptions dispensed in the 1920s. Although pharmacists increasingly relied on chemicals purchased from the manufacturer to make up prescriptions, much remained to be done secundum artem (1).

The pharmaceutical industry began to take over the production of most medications used by the medical profession in the mid-1990s. In many ways, this has provided superior service, new methods, and a vast array of innovative products that could not have been provided on a one-on-one basis. Research and development (R&D) have been the hallmarks of the pharmaceutical manufacturers. However, the very nature of providing millions of doses of a product requires that the dosage forms (capsule, tablet, suppository) and doses (individual strengths of each dose) be limited and results in a very one-sided approach to therapy. It is simply not economical for a pharmaceutical company to produce a product in 50 different conceivable doses or 15 different dosage forms to meet the needs of the entire range of persons receiving therapy. Windows of activity that meet the majority of patient needs are determined, but the very nature of the process will not be able to meet all patient needs.

We also must recognize that some individuals and their health care needs do not fall in the "windows" or "categories" of theoretical dosage strength and forms. Furthermore, large-scale manufacturers cannot tailor-make a medication for a handful of patients and do so cost effectively and meet the ever-changing needs of a given patient or institution. The pharmacist's compounding skill fills in this gap in order to meet individualized needs. By this assessment, the pharmacist, through understanding the principals of compounding and recognition of one's skill level in working secundum artem, may recommend a therapy that is not provided by the pharmaceutical industry, but one that is individualized for a specific patient's needs at a specific time.

Pharmaceutical compounding is increasing due to the impact of home health care, nonavailable drug products, orphan drugs, veterinary compounding, and biotechnology-derived drug products. Newly evolving dosage forms and therapeutic approaches suggest that compounding of pharmaceuticals and related products specifically for individual patients will become more common in pharmacy practice. Compounding pharmacy is unique as it allows one to use much of one's scientific, math, and technology background to a fuller extent than many other types of practices. Compounding pharmacists develop a special and unique relationship with their patients. They work hand-in-hand with physicians to solve problems not addressed by commercially available dosage forms.

TECHNICAL AND OTHER CONSIDERATIONS FOR COMPOUNDING

Some considerations related to compounding a prescription are as follows:

1. Is the product commercially available in the exact dosage form, strength, and packaging?
2. Is the prescription rational, i.e., ingredients, use, dose, and method of administration?
3. Are the physical, chemical, and therapeutic properties appropriate?
4. Will the compounded preparation satisfy the intent of the prescribing physician for the needs of the patient?
5. Is there an alternative dosage form, route of administration, etc. by which the patient could benefit?
6. Can the ingredient identity, quality, and purity be assured?
7. Does the pharmacist have the required training and expertise to prepare the prescription?
8. Are the proper equipment, supplies, and chemicals/drugs available?
9. Does documentation on the use, preparation, stability, administration, and storage of the preparation exist?
10. Can the pharmacist perform the necessary calculations to prepare the product?
11. Can the pharmacist project a reasonable and rational "beyond-use" date for the prescription?
12. Can the pharmacist do some basic quality control to check the preparation prior to dispensing (capsule weight variation, pH, visual observations)?

GUIDELINES AND REGULATIONS FOR COMPOUNDING

Two documents are of special importance in providing regulations and guidelines for pharmaceutical compounding. These include the *United States Pharmacopeia/National Formulary* (Chapters ≤795≥ "Pharmacy

Compounding Practices" and ≤1206≥ "Sterile Drug Products for Home Use" and other portions of the USP/NF) and the National Association of Boards of Pharmacy *Good Compounding Practices Applicable to State Licensed Pharmacies*.

United States Pharmacopeia

The following are summaries of the lengthy chapters ≤1161≥ and ≤1206≥ in the USP/NF.

Chapter ≤795≥ "Pharmacy Compounding Practices" (17) is divided into: 1) Compounding Environment, 2) Stability of Compounded Preparations, 3) Ingredient Selection and Calculations, 4) Checklist for Acceptable Strength, Quality, and Purity, 5) Compounded Dosage Forms, 6) Compounding Process, 7) Compounding Records and Documents, 8) Quality Control, and 9) Patient Counseling. The compounding environment section describes guidelines for the facilities and equipment that should be available, calibrated, maintained, and used in a compounding pharmacy. The stability section has been previously cited in this chapter, in part to provide guidelines for "beyond-use" dates to be placed on compounded preparations. The selection of ingredients has been previously discussed in this chapter and sample calculations are presented. The checklist for the USP/NF hallmarks of standards of acceptable strength, quality, and purity is presented in a series of questions to be answered. Examples of compounded dosage forms are discussed along with some precautionary statements, as appropriate. A step-by-step presentation on the compounding process is outlined to ensure uniformity of activities in preparing each preparation. Documentation is described for the Formulation Record, the Compounding Record, and the Material Safety Data Sheets (MSDS) files that should be maintained. The section ends with various aspects for patient counseling involving the proper use, storage, and evidence of instability of the compounded preparation.

Chapter ≤1206≥ "Sterile Drug Products for Home Use" covers the areas of: 1) Responsibility of the Dispensing Pharmacist, 2) Risk Levels, 3) Validation, 4) Low-Risk Operations, 5) High-Risk Operations, 6) Environmental Quality and Control, Finished Product Release Checks and Tests, 7) Storage and Expiration Dating, 8) Maintaining Product Quality and Control After it Leaves the Pharmacy, 9) Patient or Caregiver Training, and 10) Patient Monitoring and Complaint System. The compounding pharmacist dispensing any home sterile drug product is responsible for ensuring that the product has been prepared, labeled, controlled, stored, dispensed, and distributed properly. Low-risk and high-risk levels of sterile products compounding are defined with examples of each. Validation of the sterilization and aseptic processing procedures are described as related to personnel, facilities/equipment, and processes. Low-risk and high-risk operations are described, along with the validations required for each. Environmental quality and control procedures for the work area and personnel, along with suggested standard operating procedures (SOPs) and an example of an environmental monitoring program, are described. Tests and procedures for the finished product are described with the guidelines that only those products that are free from defects and meeting all quality specifications will be distributed. Guidelines are discussed for preparation, storage, and beyond-use dating after the preparation leaves the pharmacy. After the preparation leaves the pharmacy, the caregiver or patient should receive training to ensure understanding and compliance with the storage, handling, and administration of the preparations. The various aspects of the training program are outlined in this chapter. Also included are the recommendation for written policies and procedures for monitoring of patients using home-use sterile drug products and the handling and reporting of adverse events. It is evident in this chapter that the responsibility of the compounding pharmacist ranges from the activities involved in the compounding of the product through its proper storage, distribution, use, and disposal.

National Association of Boards of Pharmacy

The following is a summary of the Good Compounding Practices (GCPs) of the National Association of Boards of Pharmacy (NABP).

Subpart A contains general provisions and definitions, and sets forth the minimum current good compounding practices for the preparation of drug products by state-licensed pharmacies for dispensing and/or administration to humans or animals and includes definitions and requirements, as follows:

> Based on the existence of a pharmacist patient prescriber relationship and the presentation of a valid prescription, pharmacists may compound, in reasonable quantities, drug products that are commercially available in the marketplace. Pharmacists shall receive, store, or use drug substances for compounding that have been made in a FDA-approved facility and/or drug components that meet official compendial requirements. If neither of these requirements can be met, pharmacists shall use their professional judgment to procure alternatives.

> Pharmacists may compound drugs in very limited quantities prior to receiving a valid prescription based on a history of receiving valid prescriptions. Pharmacists shall not offer compounded drug products to other state-licensed persons or commercial entities for subsequent resale, except in the course of professional practice for a prescriber to administer to an individual patient.

Subpart B discusses the organization and personnel and the responsibilities and authority of the compounding pharmacist and other individuals involved in the compounding process.

In Subpart C, drug compounding facilities are discussed further in this section. It also discusses bulk drugs and materials as well as the compounding of sterile products, radiopharmaceuticals, and special precaution products, such as handling penicillins.

Subpart D discusses equipment and states that equipment used in the compounding of drug products shall be of appropriate design, adequate size, and suitably located to facilitate operations for its intended use and for its cleaning and maintenance.

In Subpart E control of components and drug product containers and closures are discussed. Components, drug product containers, and closures used in the compounding of drugs shall be handled and stored in a manner to prevent contamination. Their required characteristics are mentioned as well.

Subpart F, Drug Compounding Controls, explains the written procedures for the compounding of drug products in order to assure that the finished products have the identity, strength, quality, and purity they purport or are represented to possess. It also discusses some of the final quality control procedures that can be done, including, but not limited to, the following (as appropriate): 1) capsule weight variation; 2) adequacy of mixing to assure uniformity and homogeneity; and 3) clarity, completeness, or pH of solutions.

Appropriate written procedures designed to prevent microbiological contamination of compounded drug products purporting to be sterile shall be established and followed. Such procedures shall include validation of any sterilization process.

Subpart G explains labeling control of excess products. In the case where aquantity of a compounded drug product in excess of that to be initially dispensed in accordance with Subpart A is prepared, the excess product shall be labeled or documentation referenced with the complete list of ingredients (components), the preparation date, and the assigned expiration date based upon professional judgment, appropriate testing, or published data.

Subpart H discusses records and reports. Any procedures or other records required to be maintained in compliance with these good compounding practices shall be retained for the same period of time as each State requires for the retention of prescription files.

FACILITIES, EQUIPMENT, AND SUPPLIES

Compounding Facility

A separate area for traditional compounding is recommended, rather than simply cleaning off a small area of the dispensing counter. The compounding pharmacist needs a clean, neat, well-lit, and quiet working area. If aseptic compounding is considered, a "clean room" with a laminar airflow hood should be used, dependent also upon the individual state board of pharmacy requirements. The actual facility to be used will depend on the level of compounding to be done.

Adequate lighting and ventilation shall be provided in all drug-compounding areas. Potable water shall be supplied under continuous positive pressure in a plumbing system free of defects that could contribute contamination to any compounded drug product. Adequate washing facilities, easily accessible to the compounding area(s) of the pharmacy, shall be provided. These facilities shall include, but not be limited to, hot and cold water, soap or detergent, and air-driers or single-use towels.

The area(s) used for the compounding of drugs shall be maintained in a clean and sanitary condition. Trash shall be held and disposed of in a timely and sanitary manner.

Compounding Equipment

Much of the equipment used today in compounding has changed. Today, electronic balances are more often used than torsion balances. Micropipets are commonplace and ultrafreezers are sometimes required in addition to standard refrigerator–freezers. This area is constantly changing and the compounding pharmacist should be aware of the available technology necessary to prepare accurate and effective prescriptions. It is very helpful to become acquainted with the local representative for a laboratory supply company.

The equipment needed will be determined by the type and extent of the services one chooses to provide. Hospitals already utilize laminar flow hoods where aseptic compounding of sterile solutions is performed. These

same hoods can be used to compound other sterile products, such as eye drops. A balance, preferably electronic, is essential. Ointment slabs (pill tiles), along with spatulas ofdifferent types and materials, should be purchased. A few mortars and pestles (glass, ceramic, and/or plastic) should be obtained, as well as some glassware. It may not be necessary to buy a roomful of equipment, but one should purchase what is needed to start the service and build it as the service grows and expands to different arenas.

Equipment used in the compounding of drug products shall be of suitable composition so that surfaces that contact components, in-process materials, or drugproducts shall not be reactive, additive, or absorptive so as to alter the safety, identity, strength, quality, or purity of the drug product beyond that desired.

Equipment and utensils used for compounding shall be cleaned and sanitized immediately prior to use to prevent contamination that would alter the safety, identity, strength, quality, or purity of the drug product beyond that desired. In the case of equipment, utensils, and containers/closures used in the compounding of sterile drug products, cleaning, sterilization, and maintenance procedures as set forth in the NABP Model Rules for Sterile Pharmaceuticals must be followed.

Previously cleaned equipment and utensils used for compounding drugs must be protected from contamination prior to use. Immediately prior to the initiation of compounding operations, they must be inspected by the pharmacist and determined to be suitable for use.

Automatic, mechanical, or electronic equipment, or other types of equipment or related systems that will perform a function satisfactorily, may be used in the compounding of drug products. If such equipment is used, it shall be routinely inspected, calibrated (if necessary), or checked to assure proper performance.

Compounding Supplies

Throughout history, pharmacists have been using chemicals and other materials for prescription compounding. In the past, these chemicals and materials have been obtained from natural products, raw materials, and household ingredients. Today, compounding pharmacists use chemicals from various sources, depending upon their availability.

The <795> "Pharmacy Compounding Practices" monograph in the USP 24/NF 19 states as follows (17):

> A USP or NF grade drug substance is the preferred source of ingredients for compounding all drug preparations. If that is not available, the use of another high-quality source, such as analytical reagent (AR) or certified American Chemical Society (ACS) grade, is an option for professional judgment. If the substance is not an official preparation or substance, additional information, such as a certificate of analysis, needs to be obtained by the pharmacist to ensure its suitability.
>
> A manufactured drug product may be a source of an active ingredient. Only manufactured drugs from containers labeled with a batch control number and a future expiration date are acceptable as a potential source of active ingredients. When compounding with manufactured drug products, the pharmacist must consider all ingredients present in the drug product relative to the intended use of the compounded preparation.
>
> In summary, it is the responsibility of the pharmacist to select the "most appropriate" quality of chemical for compounding, beginning with the USP/NF as the first choice and, if this is not available, then descend

Table 1 Description of chemical grades

Grade	Description
Technical or commercial	Indeterminate quality
Chemically pure (CP)	More refined but still of unknown quality
USP/NF	Meets minimum purity standards; conforms to tolerances set by the *USP 23/NF 18* for contaminants dangerous to health
ACS reagent	High purity; conforms to minimum specifications set by the Reagent Chemicals Committee of the American Chemical Society
AR	Very high purity
HPLC	Solvents purified for use in HPLC; very high purity
Spectroscopic grade	Very high purity
Primary standard	Highest purity; required for accurate volumetric analysis (for standard solutions)

the list of purity grades (Table 1), using professional judgment and discretion. A certificate of analysis for the chemicals should be obtained and kept on file in the pharmacy for these selected chemicals (17, 18).

STABILITY OF COMPOUNDED PREPARATIONS

Stability is the extent to which a product retains, within specified limits and throughout its period of storage and use, the same properties and characteristics that it possessed at the time of its preparation. Chemical stability is important when selecting storage conditions (temperature, light, humidity), selecting the proper container for dispensing (glass versus plastic, clear versus amber or opaque, cap liners), and for anticipating interactions when mixing drugs and dosage forms.

Factors Affecting Stability

An important component of compounding is the consideration of factors that affect the stability of the final preparation. These factors include pH, temperature, solvent, light, air (oxygen, carbon dioxide, moisture), humidity, particle size, ionic strength, dielectric constant, polymorphism, crystallization, vaporization, and adsorption.

Types and Examples of Stability

Five types of stability are defined by the USP/NF, three of which will be described. Physical stability is concerned with the original physical properties of the preparation, and include appearance, palatability, uniformity, dissolution and suspendability. Chemical stability states that each active ingredient retains its chemical integrity and labeled potency within specified limits.

Microbiological stability states that sterility or resistance to microbial growth is retained according to the specified requirements. Antimicrobial agents that are present will retain their effectiveness within specified limits.

Beyond-Use Dating

Whereas commercially manufactured products are required to possess an "expiration date," compounded products are assigned a "beyond-use" date. Numerous sources of information can be utilized in determining an appropriate "beyond-use" date, such as chemical companies, manufacturers literature, laboratory data, journals, and published books on the subject. Generally, most pharmacists prepare/dispense small quantities of compounded products, recommend storage at room, cool, or cold temperatures, and use a conservative "beyond-use" date.

The guidelines published in the USP 24/NF 19 Chapter <795> entitled "Pharmacy Compounding Practices" state that:

> In the absence of stability information that is applicable to a specific drug and preparation, the following maximum beyond-use dates are recommended for nonsterile compounded drug precautions that are packaged in tight, light-resistant containers and stored at controlled room temperature unless otherwise indicated.
>
> For nonaqueous liquids and solid formulations (where the manufactured drug product is the source of active ingredient), the beyond-use date is not later than 25% of the time remaining until the product's expiration date or 6 months, whichever is earlier.
>
> A USP or NF substance is the source of active ingredient-the beyond-use date is not later than 6 months. For water-containing formulations (prepared from ingredients in solid form)-the beyond-use date is not later than 14 days when stored at cold temperatures.
>
> For all other formulations-the beyond-use date is not later than the intended duration of therapy or 30 days, whichever is earlier. These beyond-use date limits may be exceeded when there is supporting valid scientific stability information that is directly applicable to the specific preparation (i.e., the *same* drug concentration range, pH, excipients, vehicle, water content, etc.) (17).

COMPOUNDING QUALITY CONTROL

Physical Tests

Pharmacists can perform a number of physical quality control tests to ensure the uniformity and accuracy of many small-scale compounded preparations. These quality control tests include individual dosage unit weights, average individual dosage unit weights, total product weight, pH, and physical observations such as appearance, taste, and smell.

Physical Observations

Physical observations can include color, clarity, uniform distribution, hardening, brittleness, softening, discoloration, expansion/distortion, caking, odor, precipitation, discoloration, haziness, gas formation, clarity, breaking, creaming, difficulty in resuspending, consistency, grittiness, dryness, shrinkage, water evaporation, shriveling, and the presence of oil stains on packaging.

Sterile Products Testing

If appropriate, due to the number of sterile preparations compounded, products may be tested for sterility and the effectiveness of incorporated preservatives, if present. This may be done either at the pharmacy or in a contract laboratory.

Pyrogen Testing

Pyrogen testing should be done especially if sterile preparations are made from nonsterile bulk materials. This testing can be done either at the pharmacy or in a contract laboratory.

Contract Analytical Laboratories

Contract analytical testing can be utilized for purity, potency, sterility, and pyrogenicity testing. The frequency of testing is generally related to the volume and frequency of product preparation.

FLAVORS, SWEETENERS, AND COLORS

Preparation of an Asthetic Product

Flavoring, sweetening, and coloring are important to enhance patient compliance when medications are administered orally. Oftentimes, these can be adjusted to meet the preferences of the patient.

Basics and Examples of Flavoring

Pharmacists must be familiar with the four primary tastes (sweet, sour, salty, and bitter) and be aware of the correlations between select chemical properties and taste and odor. Using this information, they can use a number of approaches to prepare an acceptable product to minimize the bad taste of drugs. These approaches include blending, overshadowing, physical methods (insoluble compounds, emulsification, effervescence, viscosity), chemical methods (adsorption, complexation), and physiological techniques (cooling due to negative heat of solution anesthetic action of some ingredients). Also, flavor intensifiers can be used, including citrus enhancers, such as citric, maleic, or tartaric acids.

Basics and Examples of Sweetening

A number of different types of sweeteners, caloric and noncaloric, are available, depending upon the specific prescription and patient. Some sweeteners have aftertastes that must also be considered. Today, patients also can have their choice of natural or synthetic sweeteners.

Basics and Examples of Coloring

Coloring is not always necessary but may be of value in certain medications. For example, oral liquids are generally colored with a dye that matches the flavor of the medication. Pharmacists must be aware of the different oil, alcohol, and water solubilities of the dyes they use.

PRESERVATION, STERILIZATION, AND DEPYROGENATION

Methods of Preservation

Some compounded preparations are naturally preserved, as in the case of some syrups and elixirs. Others require the addition of a preservative. Preservatives are commonly added to products to minimize microbial growth, as in the case of oral liquids, topicals, and multidose parenterals.

Physicochemical Considerations in Preservation

A preservative is selected based upon its characteristics, including concentration, pH, taste, odor, and solubility.

Preservative Effectiveness Testing

In some situations, it is advisable to have a preservative effectiveness test conducted on a preparation that may

require routine compounding or may require an extended storage period.

Methods of Sterilization

Compounding pharmacists routinely use in-process sterilization, such as sterile filtration, or terminal sterilization, such as autoclaving or dry-heat sterilization. In some situations, combinations of these methods may be used along with chemical sterilization.

Methods of Depyrogenation

Depyrogenation methods used by compounding pharmacists include dry heat and rinsing with Sterile Water for Injection, USP.

COMPOUNDING PHARMACEUTICAL SOLIDS

Powders and Granules

Powders are thorough mixtures of dry, finely divided drugs and excipients that are intended for internal or external use. Granules are dosage forms that consist of particles ranging in size from about 4–10 mesh. Both powders and granules are easy to use and are easy to compound. An example formula of a currently compounded powder includes the following:

Rx Misoprostol	600 g
Lidocaine hydrochloride	500 mg
Polyox WSR-301	2.45 g
Methocel E4M Premium	22.05 g

Capsules

Capsules are dosage forms in which unit doses of powder, semisolid, or liquid drugs are enclosed within either a hard or a soft envelope or shell. Examples of currently compounded capsules include the following with the contents either as powders, in oil or in a semisolid-fill capsule, as well as modified strength capsules:

Rx Dextromethorphan Hydrobromide 30 mg and Morphine Sulfate 10 mg Capsules (#100)	
Dextromethorphan hydrobromide	3 g
Morphine sulfate	1 g
Lactose	35.5 g
Capsule size #1	#100

Rx Triple Estrogen 2.5 mg Slow-Release Capsules (#100)	
Estriol	200 mg
Estrone	25 mg
Estradiol	25 mg
Methocel E4M Premium	10 g
Lactose	23.75
Capsule size #1	#100

Rx Triple Estrogen 2.5 mg in Oil Capsules (#100)	
Estriol	200 mg
Estrone	25 mg
Estradiol	25 mg
Peanut oil	20 ml (18.38 g)
Capsules size #1	#100

Rx Triple Estrogen 2.5 mg Semisolid-Filled, Hard-Gelatin Capsules (#100)	
Estriol	200 mg
Estrone	25 mg
Estradiol	25 mg
Polyethylene glycol 1450	20 g
Polyethylene glycol 3350	20 g
Capsules size #1	#100

Tablets

Tablets are solid dosage forms that are generally either compressed or prepared by a sintering process, which includes sublingual, buccal, chewable, effervescent, and compressed tablets. Some of these can be easily compounded. An example of a tablet triturate is as follows:

Rx Sodium Fluoride 2.2 mg Tablet Triturates (#100)	
Sodium fluoride	220 mg
Sucrose, powdered	1.15 g
Lactose, hydrous	4.63 g

Lozenges/Troches

Lozenges/troches are solid preparations designed to dissolve or disintegrate slowly in the mouth. Their base is usually flavored and sweetened. Examples of compounded troches include anesthetic (lidocaine), hormonal (testosterone), analgesic (ketamine), and antifungal (nystatin) preparations.

Rx Testosterone 10 mg Troches (#24)	
Testosterone	240 mg
Aspartame	500 mg
Silica gel	480 mg
Acacia	360 mg
Flavor	qs
Polyethylene glycol 1450	23 g

Rx Pediatric Chewable Gummy Gels

Active drug	qs
Bentonite	500 mg
Aspartame	550 mg
Acacia powder	500 mg
Citric acid monohydrate	700 mg
Flavor	qs
Gummy gel base	26.6 g

Rx Gummy Gel Base

Gelatin	43.4 g
Glycerin	155 ml
Purified water	21.6 ml

Rx Nystatin Popsicles (#10)

Nystatin powder	2,500,000 units
Sorbitol 70% solution	20 ml
Simple syrup	50 ml
Flavor	qs
Purified water qs	300 ml

Rx Tetracaine 20 mg Lollipops (#30)

Tetracaine HCl	600 mg
Lemon essence	0.5 ml
Green food color	2 ml
Sucrose	150 g
Potassium bitartrate	500 mg
Purified water	55 ml

Suppositories

Suppositories are solid dosage forms that are used to administer medicine through the rectum, vagina, or urethra. They are of different sizes or shapes, depending upon the body orifice for their administration. Examples of compounded suppositories include the antinauseant combinations (lorazepam, diphenhydramine, haloperidol, and metoclopramide), analgesic (morphine), antifungal, and hemorrhoidal (lidocaine, tannic acid) preparations.

Rx Fluconazole 200 mg Vaginal Suppositories

Fluconazole	200 mg
Polyethylene glycol base	qs

Rx Morphine Sulfate Slow-Release Suppositories (#1)

Morphine sulfate	50 mg
Alginic acid	25%
Witepsol H-15	qs

Sticks

Sticks are a convenient form of administering topical medications and come in different sizes and shapes. They are readily transportable and can be easily compounded.

Rx Gralla Type Antiemetic Suppositories

Ingredient	*#1*	*#2*	*#3*	*#4*	*#5*	*#6*	*#7*
Metoclopramide HCl	10	—	20	10	40	20	20
Haloperidol	0.5	5	—	—	1	1	—
Diphenyhydramine HCl	—	25	25	—	25	25	25
Dexamethasone	—	—	10	—	10	10	5
Lorazepam	0.5	2	—	—	1	—	—
Diazepam	—	—	—	5	—	—	—
Hydroxyzine HCl	25	—	—	—	—	—	—
Promethazine HCl	—	—	—	25	—	—	—
Benztropine mesylate	—	—	—	—	1	—	—
Silicon dioxide	20	30	20	15	—	—	—
Fatty acid base qs	2g		2g	2g	2g	2g	2g
Polyethylene glycol base qs	—	2g	—	—	—	—	—

Examples of compounded sticks include those containing antivirals for herpes and emollients/sunscreens for environmental exposure.

Rx Fluorouracil 5% Topical Stick (25-g tubes)

Fluorouracil	5 g
Polyethylene glycol 3350	27 g
Polyethylene glycol 300	68 g

Rx Acyclovir Stick with Sunscreen (five 5-g tubes)

Acyclovir 200 mg capsules	#5
para-Aminobenzoic acid	150 mg
Silica gel, micronized	120 mg
Polyethylene glycol 3350	6.5 g
Polyethylene glycol 300	15 ml

COMPOUNDING PHARMACEUTICAL LIQUIDS

Solutions

Solutions are liquid preparations that contain one or more drug substances molecularly dispersed in a suitable solvent or a mixture of mutually miscible solvents. Solutions include those for use topically as well as internally.

Rx Dexamethasone and Lidocaine Solution for Iontophoresis (100 ml)

Dexamethasone sodium phosphate	200 mg
Lidocaine hydrochloride	1 g
Sterile water for injection	100 ml

Rx Buprenorphine Hydrochloride 150 mg/100 ml Nasal Spray (100 ml)

Buprenorphine hydrochloride	150 mg
Glycerin	5 ml
Methylparaben	200 mg
0.9% Sodium chloride injection	95 ml

Examples of compounded liquids include topicals (wart solutions), oral syrups and elixirs, nasal solutions, otic solutions, iontophoretic solutions (dexamethasone sodium phosphate), and many others.

Suspensions

Suspensions are two-phase systems that consist of a finely divided solid dispersed in a liquid, solid, or gas. They are appropriate when the drug to be incorporated is not sufficiently soluble in an ordinary solvent or cosolvent system. They are used orally and topically. Examples of compounded suspensions include many pediatric oral liquids where a commercial pediatric dosage form is not available. Commercial tablets and capsules are formulated into a vehicle for the patient and can be individually flavored to the patient's preferences.

Rx Indomethacin 4% Topical Spray (100 ml)	
Indomethacin	4 g
Hydroxypropyl cellulose	200 mg
Sodium lauryl sulfate	100 mg
Purified water	10 ml
Alcohol, 95% qs	100 ml

Rx Testosterone 10 mg/0.1 ml Sublingual Drops (10 ml)	
Testosterone	1 g
Saccharin	100 mg
Silica gel	200 gm
Flavor	qs
Almond oil qs	10 ml

Emulsions

Emulsions are heterogeneous systems consisting of at least one immiscible liquid that is intimately dispersed in another liquid in the form of droplets or globules, whose diameters generally exceed 0.1 micron. They are also thermodynamically unstable mixtures of two essentially immiscible liquids and an emulsifying agent that helps hold them together. Examples of compounded emulsions include those for both topical and oral used. Topical emulsions include creams and even liposomal preparations. Compounded emulsions include preparations for both oral and topical use. This category also includes the pluronic-lecithin-organogels, which are penetration-enhancing gels.

Rx Emulsion Base	
Mineral oil, heavy	25 ml
Isopropyl myristate	25 ml
Polysorbate 80	7 ml
Methylparaben	200 mg
Propylparaben	100 mg
Purified water qs	100 ml

Rx Ketamine 10% in Pluronic Lecithin Organogel	
Ketamine hydrochloride	10 g
Isopropyl palmitate:Soy lecithin 1:1	20 g
Plutonic F127 20% gel qs	100 ml

COMPOUNDING PHARMACEUTICAL SEMISOLIDS

Ointments and Pastes

Ointments are semisolid preparations that are intended to be applied externally to the skin or mucous membranes. They soften or melt at room temperature. Pastes are thick, stiff ointments that ordinarily do not flow at body temperature and thus protect and coat the areas to which they are applied. Examples of compounded ointments and pastes include the following:

Note: The testosterone-menthol eutectic mixture can be prepared by mixing 31.6 g of testosterone with 68.4 g menthol, using sufficient methyl alcohol to dissolve them both and allowing the alcohol to evaporate to dryness.

Rx Testosterone–Menthol Eutectic Ointment (2% Testosterone)	
Testosterone–menthol eutectic mixture	6.33 g
Hydrophilic petrolatum	93.67 g

Rx Aluminum Acetate Paste (100 g)	
Aluminum acetate solution	17 ml
Anhydrous lanolin	34 g
Lassar's Plain Zinc Paste	49 g

Creams

Creams are opaque, soft solids or thick liquids intended for external application. Creams may contain medications dissolved or suspended in water-soluble or vanishing cream bases and can be either water-in-oil or oil-in-water. Examples of creams are as follows:

Rx Progesterone 5% Cream	
Micronized progesterone	5 g
Glycerin	qs
Hydrophilic ointment	95 g

Note: Commercial oil-in-water vehicles can be used and the quantity of progesterone is variable.

Gels

Gels are semisolid systems that consist of suspensions made up of either small inorganic particles or large organic molecules interpenetrated by a liquid. Some gels are clear and others are turbid since their ingredients may or not be completely molecularly dispersed or they may from aggregates, which disperse light. Examples of compounded gels include many topical, oral cavity, and even rectally administered preparations, such as the following:

Rx Piroxicam Topical Gel

Hydroxypropylcellulose	1.75 g
70% isopropyl alcohol	98.25 ml
Propylene glycol	4.1 ml
Polysorbate 80	1.7 ml
Piroxicam 20-mg capsules	25 capsules
(Piroxicam powder can be used, if available.)	

Rx Ketoprofen, Topical Gel Cyclobenzaprine and Lidocaine

Ketoprofen	10 g
Cyclobenzaprine hydrochloride	1 g
Lidocaine	5 g
Propylene glycol	10 ml
Sorbic acid	200 mg
Lecithin:isopropyl palmitate solution	20 g

COMPOUNDING STERILE PREPARATIONS

Ophthalmics

Ophthalmic preparations are sterile, free from foreign particles, and prepared especially for instillation into the eye. They include solutions, suspensions, and ointments. Examples of compounded ophthalmics include drugs such as acetylcysteine, acyclovir, alteplase, amikacin, amphotericin B, ascorbic acid, bacitracin, calcium gluconate, penicillins, cephalosporins, aminoglycosides, cromolyn, cyclosporin, deferoxamine, anti-inflammatory corticosteroids, chelating agent, oncology agents, and numerous others prepared as both solutions and ointments.

Rx Acetylcysteine 15% Ophthalmic Solution

Acetylcysteine	15 g
Sterile water for injection qs	100 ml
Sodium hydroxide to pH of 6 to 7.5	

Inhalation Solutions

Inhalation solutions are designed to deliver a drug into the respiratory tree of a patient for either a local or systemic effect. Examples of compounded inhalation solutions include individual and combinations of albuterol, cromolyn, morphine sulfate, corticosteroids, ipratropium, metaproterenol, terbutaline, and others.

Rx Morphine Sulfate 0.25% Inhalation Solution

Morphine sulfate	250 mg
Citric acid, hydrous	100 mg
Sterile water for injection, qs	100 ml

Rx Albuterol Sulfate and Ipratropium Bromide Inhalation Solution

Albuterol sulfate	100 mg
Ipratropium bromide	16.7 mg
Benzalkonium chloride 50% solution	0.003 ml
0.9% Sodium Chloride Injection qs	100 ml

Parenterals

Parenterals are products that are administered to the body by injection. They must be sterile, nonpyrogenic, and particulate-free. Examples of compounded parenterals include high-dose analgesics for patient-controlled analgesia (morphine sulfate 50 mg/ml), antiemetic injections, fentanyl and bupivacaine injections for ambulatory pump reservoirs, oncology combinations, and others.

Rx Reglan, Ativan and Compazine Injection

Reglan (5 mg/ml)	30 ml	150 mg
Ativan (2 mg/ml)	0.5 ml	1 mg
Mannitol 25%	50 ml	12.5 mg
Compazine (5 mg/ml)	2 ml	10 mg
5% Dextrose injection		50 ml

Rx Fentanyl Citrate 1.25 g/ml, Bupivacaine Hydrochloride 0.4375 mg/ml, Epinephrine Hydrochloride 0.69 g/ml

Fentanyl citrate 50 μg/ml	2.5 ml
Bupivacaine hydrochloride, 0.5%	8.75 ml
Epinephrine hydrochloride, 1:100,000	6.9 ml
0.9% sodium chloride injection	81.85 ml

Rx TPN Solution

50% Dextrose injection	500 ml
Amino acids 8.5% with Lytes	500 ml
Lipids 10%	200 ml
Calcium gluconate	1 g
Magnesium sulfate	ss2 g
Trace elements	1 unit
M.V.I.-12	1 unit

COMPOUNDING WITH BIOTECHNOLOGY PREPARATIONS

Definitions

Biotechnology preparations are those that are developed using the techniques of engineering and technology with living organisms. Biotechnology presents compounding pharmacists with a unique and new source of therapeutic agents that may require their special expertise.

Types of Preparations

Biotechnology products differ in their method of preparation and potential problems presented in their formulation. Pharmacists involved in compounding with biologically active proteins will be interested in their stabilization, formulation, and delivery. Most of the biotechnology products currently are proteins but some may soon be smaller peptide-like molecules.

Physicochemical Considerations

In working with biotechnology-derived drugs, the compounding pharmacist must be cognizant of both the active drug constituent and the total drug delivery system or carrier. Proteins are generally very potent and used in very low concentrations. Pharmacists must be aware of the vehicle, buffer, and stabilizer requirements for these preparations, including the use of surfactants, amino acids, polyhydric alcohols, fatty acids, proteins, antioxidants, reducing agents, and metal ions. Proper pH, chelating agents, preservatives and tonicity-adjusting agents must be considered.

Quality Control and Stabiliy

One must be aware of the factors involved in handling proteins in order to retain a drug's biologic activity up to the time when it is administered to the patient. Proteins are inherently unstable molecules and their degradation profiles can be very complex. Compounding pharmacists may be involved in the selection of an appropriate vehicle for drug delivery, individualizing dosages, administering drugs through novel drug delivery systems, preparing drugs for delivery through these systems, monitoring their efficacy, and counseling patients on their use.

An example of a compounded prescription using a biotechnology-derived product is as follows:

Rx Tissue Plasminogen Activator 25 mg/100 L
Ophthalmic Solution

Tissue plasminogen activator	20 mg vial
0.9% Sodium chloride injection	60 ml
Sterile water for injection	20 ml

COMPOUNDING VETERINARY PREPARATIONS

Guidelines for Veterinary Compounding

Veterinary compounding can be considered when there are no effective FDA-approved products available, when available dosage forms are inappropriate, when multiple and concurrent disease states are present, when an additive therapeutic effect could be obtained from simultaneous administration of two or more products or to minimize side effects, when economic realities would preclude treatment with the approved product, and when compounding would encourage compliance of dosage/therapeutic regimens.

Considerations in Veterinary Compounding

Most drugs that are FDA-approved are specified for certain species, either food producing or for a large target population. If veterinarian pharmaceutical companies do not perceive a sufficiently large market for a product, they will not seek approval for products. This has left a large vacuum, or a potential market, to be filled by compounding pharmacists. There are no FDA-approved products for exotic species due to the limited market and there are only limited FDA-approved products for some of the more common species. Veterinarians need patient-specific products and pharmacists know how to prepare these products. Consequently, a team approach has developed to the benefit of the veterinarian, pharmacist, and animal patient.

Questions that often arise include the following. What is the overall goal of the treatment of this animal? Are there any commercially available products that can be used? What are the regulatory concerns? Is this a food or a milk-producing animal? Will there be a residue problem? What do we know about the physical and chemical compatibility of these drugs? What do we know about the stability of these drugs before, during, and after the compounding process? What do we know about the pharmacokinetics of the active ingredients? Are personnel going to be at risk from handling the drug during compounding or while using the compounding form?

Examples of some veterinary preparations are as follows:

Rx Acetylcysteine, Gentamicin and Atropine Solution	
Acetylcysteine	720 mg
Gentamicin (as gentamicin sulfate)	36 mg
Atropine sulfate	36 mg
Sterile water qs	15 ml

Rx 4-Methyl-pyrazole Solution	
4-Methyl-pyrazole	1 g
Polyethylene glycol 400	9 ml
Bacteriostatic water for injection qs	20 ml

SUMMARY

Pharmacy compounding provides pharmacists with a unique opportunity to practice their time-honored profession. It will become an even more important part of pharmacy practice in the future, and include pharmacists involved in community, hospital, nursing home, home health care, veterinary, and specialty practices. Pharmaceutical compounding is a practice where the clinical expertise of pharmacists can be merged with the scientific expertise of pharmacists to make pharmaceutical care a reality.

REFERENCES

1. Allen, Loyd V., Ed. *The Compact Oxford English Dictionary*, 2nd Ed.; Oxford University Press, Inc.: New York, 1991.
2. Allen, Loyd V., Ed. *American Heritage Dictionary of the English Language*, 3rd Ed.; 1992; In Electronic Form in Microsoft Bookshelf'95, Microsoft Corporation, 1995.
3. Allen, Loyd V., Ed. *Webster's Revised Unabridged Dictionary of the English Language,* G & C Merrian Company: Springfield, MA, 1913; 1075.
4. Williamson, R.E.; Kabat, H.F. Job Satisfaction among Minnesota Hospital Pharmacists. Am. J. Hosp. Pharm. **1972**, *29*, 942–946.
5. Humphrys, P.; O'Brien, G.E. The Relationship between Skill Utilization, Professional Orientation and Job Satisfaction for Pharmacists. J. Occupational Behav. **1986**, *59*, 315–326.
6. Johnson, C.A.; Hammel, R.J.; Heinen, J.S. Levels of Satisfaction among Hospital Pharmacists. Am. J. Hosp. Pharm. **1977**, *34*, 341–247.
7. Olson, D.S.; Lawson, K.A. Relationship between Hospital Pharmacists' Job Satisfaction and Involvement in Clinical Activities. Am. J. Health-Syst. Pharm. **1996**, *53*, 281–284.
8. Letendre, W.R.; Shepherd, M.D.; Brown, C.M. Comparison of Job Satisfaction for Compounders and Concompounders. Int. J. Pharmaceutical Compounding **1998**, *2* (6), 455–462.
9. Penna, R. What Makes Pharmacists Different?. Am. J. Pharmaceutical Ed. **1997**, *61* (Spring), 103.
10. *Good Compounding Practices Applicable to State Licensed Pharmacies* NABP: Park Ridge, IL, .
11. Popovich, N.G. Ambulatory Patient Care. *Remington: The Science and Practice of Pharmacy*, 19th Ed.; Gennaro, A.R., Ed.; Mack Publishing Co.: Easton, PA, 1995; 1695–1719.
12. Raehl, C.L.; Bond, C.A.; Pitterle, M.E. Ambulatory Pharmacy Services Affiliated with Acute Care Hospitals. Pharmacotherapy **1993**, *13* (6), 618–625.
13. Goode, M.A.; Gums, J.G. Therapeutic Drug Monitoring in Ambulatory Care. Ann. Pharmacother. **1993**, *27*, 502–505.
14. Sundberg, J.A. Extemporaneous Compounding in the Hospital Pharmacy. Int. J. Pharmaceutical Compounding **1997**, *1* (5), 314–317.
15. Proc. J. Amer. Vet. Med. Assoc. **1994**, *204* (2), 189–305.
16. Shaw, S.M. Introduction to Nuclear Pharmacy. Int. J. Pharmaceutical Compounding **1998**, *2* (6), 424–425.
17. *United States Pharmacopeia XXIV/National Formulary 19;* US Pharmacopeial Convention, Inc.: Rockville, MD, 2000; 2128–2143, 2698–2704.
18. Food and Drug Modernization Act of 1997.